Complete Summary

GUIDELINE TITLE

Guidelines for the management of chronic kidney disease in HIV-infected patients: recommendations of the HIV Medicine Association of the Infectious Diseases Society of America.

BIBLIOGRAPHIC SOURCE(S)

Gupta SK, Eustace JA, Winston JA, Boydstun II, Ahuja TS, Rodriguez RA, Tashima KT, Roland M, Franceschini N, Palella FJ, Lennox JL, Klotman PE, Nachman SA, Hall SD, Szczech LA. Guidelines for the management of chronic kidney disease in HIV-infected patients: recommendations of the HIV Medicine Association of the Infectious Diseases Society of America. Clin Infect Dis 2005 Jun 1;40(11):1559-85. [238 references] PubMed

GUIDELINE STATUS

This is the current release of the guideline.

COMPLETE SUMMARY CONTENT

SCOPE
METHODOLOGY - including Rating Scheme and Cost Analysis
RECOMMENDATIONS
EVIDENCE SUPPORTING THE RECOMMENDATIONS
BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS
CONTRAINDICATIONS
QUALIFYING STATEMENTS
IMPLEMENTATION OF THE GUIDELINE
INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES
IDENTIFYING INFORMATION AND AVAILABILITY
DISCLAIMER

SCOPE

DISEASE/CONDITION(S)

- Chronic kidney disease
- Human immunodeficiency virus (HIV) infection

GUIDELINE CATEGORY

Diagnosis
Evaluation

Management
Screening

CLINICAL SPECIALTY

Family Practice
Hematology
Infectious Diseases
Internal Medicine
Nephrology
Pediatrics

INTENDED USERS

Advanced Practice Nurses
Allied Health Personnel
Nurses
Patients
Physician Assistants
Physicians

GUIDELINE OBJECTIVE(S)

To address the clinical issues involved in both adults and children with human immunodeficiency virus (HIV)-related renal disease

TARGET POPULATION

Human immunodeficiency virus (HIV)-infected patients (adults and children) with chronic kidney disease

INTERVENTIONS AND PRACTICES CONSIDERED

Screening and Diagnostic Evaluation

1. Qualitative assessment for risk of kidney disease (e.g., race, family history, $CD4^+$ lymphocyte count, human immunodeficiency virus [HIV]-1 ribonucleic acid [RNA] level, history of nephrotoxic medications, comorbidities)
2. Urine analysis for proteinuria
3. Calculated estimate of renal function (estimation of creatinine clearance or glomerular filtration rate)
4. Annual follow up
5. Blood pressure measurement
6. Quantification of proteinuria (albumin-to-creatinine ratio or protein-to creatinine-ratio)
7. Renal ultrasound
8. Renal biopsy

Management/Treatment

1. Referral to nephrologist

2. Control of hypertension
    - Angiotensin-converting enzyme (ACE) inhibitors
    - Angiotensin receptor blockers (ARBs)
3. Dialysis
4. Arteriovenous fistulae placement
5. Renal transplantation
6. Highly active antiretroviral therapy (HAART)
7. Prednisone
8. Adjustment of antiretroviral medication and antimicrobial agent dosing
9. Use of recombinant human erythropoietin
10. Use of 1,25-dihydroxy vitamin D3 or its analogues
11. Hepatitis B vaccination (Recombivax HB, Engerix B) and checking of anti-hepatitis B surface antigen titers following vaccination
12. Streptococcus pneumoniae vaccination (Pneumovax, Pnu-imune 23)
13. Influenza virus vaccination
14. Hepatitis A vaccination

MAJOR OUTCOMES CONSIDERED

- Renal function
- Side effects of medications
- Incidence of chronic kidney disease
- Incidence of human immunodeficiency virus (HIV)-associated nephropathy
- Survival
- Morbidity and mortality

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Searches of Electronic Databases

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

The evidence for these guidelines was collected using MEDLINE searches of the relevant literature and reviews of pertinent abstracts (all in the English language) presented at both major infectious diseases and nephrology society meetings from January 2000 through February 2004.

NUMBER OF SOURCE DOCUMENTS

Not stated

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Weighting According to a Rating Scheme (Scheme Given)

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

Quality of Evidence

I. Evidence from at least one properly randomized, controlled trial
II. Evidence from at least one well-designed clinical trial without randomization, from cohort or case-controlled analytic studies (preferably from more than one center), from multiple time-series studies, or from dramatic results of uncontrolled experiments
III. Evidence from opinions of respected authorities based on clinical experience, descriptive studies, or reports of expert committees

METHODS USED TO ANALYZE THE EVIDENCE

Systematic Review

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

Not stated

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Expert Consensus

DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS

Not stated

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Strength of Recommendation

A. Good evidence to support a recommendation for use
B. Moderate evidence to support a recommendation for use
C. Poor evidence to support a recommendation
D. Moderate evidence to support a recommendation against use
E. Good evidence to support a recommendation against use

COST ANALYSIS

A formal cost analysis was not performed and published cost analyses were not reviewed.

METHOD OF GUIDELINE VALIDATION

External Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

Not stated

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

Definitions of the levels of evidence (I-III) and grades of recommendation (A-E) are repeated at the end of the Major Recommendations field.

Screening and Initial Evaluations

All patients at the time of human immunodeficiency virus (HIV) diagnosis should be assessed for existing kidney disease with a screening urine analysis for proteinuria and a calculated estimate of renal function (C-III).

If there is no evidence of proteinuria at initial evaluation, patients at high risk for the development of proteinuric renal disease (i.e., African American persons, those with $CD4^+$ cell counts <200 microL or HIV RNA levels >4,000 copies/mL, and those with diabetes mellitus, hypertension, or hepatitis C virus coinfection) should undergo annual screening (B-II). Renal function should be estimated on a yearly basis to assess for changes over time (B-II).

Additional evaluations (including quantification of proteinuria, renal ultrasound, and potentially renal biopsy) and referral to a nephrologist are recommended for patients with proteinuria of grade $\geq$1+ by dipstick analysis or glomerular filtration rate (GFR) <60 mL/min per 1.73 m^2 (B-II).

Management

In HIV-infected patients with evidence of nephropathy, blood pressure should be controlled to a level no higher than 125/75 mm Hg (B-III), with the initial preferential use of angiotensin-converting enzyme (ACE) inhibitors or angiotensin receptor blockers (ARBs) for those patients with proteinuria (B-II). Calcium channel blockers should be avoided in patients receiving protease inhibitors (D-II).

Dialysis and the placement of arteriovenous fistulae (native fistulae preferred [A-II]) should not be withheld for patients solely because of HIV infection (A-II)

Renal transplantation may be considered for patients with end-stage renal disease (ESRD) if provided in a supervised clinical trial or at centers with adequate experience in this area (C-III).

Patients with HIV-associated nephropathy (HIVAN) should be treated with highly active antiretroviral therapy (HAART) at diagnosis (B-II). HAART should not be withheld from patients simply because of the severity of their renal dysfunction (B-III).

Addition of ACE inhibitors, ARBs, and/or prednisone should be considered in patients with HIVAN if HAART alone does not result in improvement of renal function (B-II).

Antiretroviral Dosing And Renal Toxicities

Appropriate reduction of dosing for antiretrovirals that are primarily renally eliminated is warranted (C-III), with additional doses given after hemodialysis for those drugs that are readily removed by dialysis (B-II).

Nucleoside analogues should not be withheld in patients with reduced renal function for fear of the development of lactic acidosis (D-III).

Patients receiving indinavir should drink at least 1.5 L of water daily to prevent stone formation (B-III). Periodic monitoring of renal function and pyuria should be performed during the first 6 months of indinavir therapy and biannually thereafter (B-II), although routine screening for crystalluria is not warranted unless there is a suspicion of nephrolithiasis (B-II). Indinavir need not be withheld from patients with reduced renal function (C-III). In patients who develop indinavir nephrolithiasis, it would be reasonable to restart indinavir therapy once rehydration is achieved (B-III). Patients who develop indinavir-induced hypertension, pyuria, rhabdomyolysis, or renal insufficiency (acute or chronic) should permanently discontinue use of this drug (B-III).

Patients receiving tenofovir who have a GFR <90 mL/min per 1.73 m^2, patients receiving other medications eliminated via renal secretion (e.g., adefovir, acyclovir, ganciclovir, or cidofovir), patients with other comorbid diseases (e.g., diabetes or hypertension), or patients receiving ritonavir-boosted protease inhibitor regimens should be monitored at least biannually for measurements of renal function, serum phosphorus, and urine analysis for proteinuria and glycosuria (B-III).

HIV Antiretroviral Dosing Recommendations

A summary of dosing recommendations for patients with chronic kidney disease (CKD)/ESRD is provided in Table 3 of the original guideline document.

Renal Dosing of Antibiotics Commonly Used in HIV Care

Many of the antimicrobials commonly used to prevent and treat opportunistic infections such as Pneumocystis jiroveci pneumonia, Toxoplasma encephalitis, and Mycobacterium avium intracellulare infections require dose reduction in the HIV-infected patient with CKD because of their renal elimination. Recommended dosing data for these drugs are available in Table 4 of the original guideline document.

HIV Infection And CKD in the Pediatric and Adolescent Populations

In children without evidence of existing renal disease, screening evaluation for the development of HIVAN is similar to that proposed earlier for adults and should include complete urinalysis and testing to determine serum electrolyte levels, blood urea nitrogen levels, and creatinine levels every 6 months (C-III).

Pediatric HIVAN and other proteinuric nephropathies in HIV-infected children should be treated with HAART; referral to a nephrologist and the addition of ACE-

inhibition should also be considered for patients with more severe proteinuria (grade ≥1+ by urine dipstick analysis or a protein-to-creatinine ratio ≥0.2 g/g for 3 separate specimens) (C-III). Steroid use is not recommended for this population (D-II).

Special Topics

Use of recombinant human erythropoietin should be considered in patients with hemoglobin levels 2 g/dL less than the lower limit of normal; the therapeutic hemoglobin target is a hemoglobin level of 11 to 12 g/dL (C-III).

Analogous to the general population with CKD, all HIV-infected ESRD patients with secondary hyperparathyroidism (serum calcium level, <9.5 mg/dL; serum phosphorus level, <4.6 mg/dL; and serum parathyroid hormone level, >35 pcg/mL) should be treated with 1,25-dihydroxy vitamin D3 or its analogues (C-III).

HIV-infected patients requiring hemodialysis should have anti-HBs titers checked after receiving a standard primary series of 3 hepatitis B vaccinations and should receive a fourth injection if these titers are <10 IU/L (B-II).

Vaccinations Recommended for HIV-Infected Adults with Chronic Kidney Disease

Pathogen	Recommendation(s)
Streptococcus pneumoniae	Pneumovax[a] or Pnu-Imune[b] 23 administered in a single 0.5-mL subcutaneous or intramuscular dose if $CD4^+$ cell count ≥200 cells/mm^3. Additional vaccination is recommended for patients initially vaccinated at a $CD4^+$ count <200 cells/mm^3 whose $CD4^+$ count increases to ≥200 cells/mm^3. It is preferable to vaccinate such individuals before development of end-stage renal disease. Patients should be revaccinated after 5 years.
Influenza virus	All patients should be vaccinated annually.
Hepatitis A virus	Patients who are negative for anti-hepatitis A virus and patients at increased risk for hepatitis A virus infection (e.g., illicit drug users, men who have sex with men, and patients with chronic liver disease [including chronic hepatitis B or hepatitis C]) should be vaccinated.
Hepatitis B virus	
Patients of all ages	For monitoring, check antibody to hepatitis B surface antigen (anti-HBs) titers 1-2 months after the last primary vaccine dose is administered (an adequate response is ≥10 mIU/mL). Revaccinate those patients who do not respond with 3 doses. For those patients who do respond, follow anti-HBs levels semiannually; if anti-HBs levels are <10 mIU/mL, administer a booster dose.
Patients aged >20 years Predialysis	Administer Recombivax HB[a] at a dose of 10 micrograms at 0, 1, and 6 months or Engerix-B[c] at a dose of 20 micrograms intramuscularly (im) at 0, 1, and 6 months.

Pathogen	Recommendation(s)
Dialysis dependent	Administer Recombivax HB[a] at a dose of 40 micrograms at 0, 1, and 6 months or Engerix-B[c] at a dose of 40 micrograms im at 0, 1, and 6 months.
Patients aged <20 years	Administer Recombivax HB[a] at a dose of 5 micrograms at 0, 1, and 6 months or Engerix-B[c] at a dose of 10 micrograms im at 0, 1, and 6 months.

[a]Merck
[b]Lederle
[c]SmithKline Beecham Biologicals

Definitions

Quality of Evidence

I. Evidence from at least one properly randomized, controlled trial
II. Evidence from at least one well-designed clinical trial without randomization, from cohort or case-control analytic studies (preferably from more than one center), from multiple time-series studies, or from dramatic results of uncontrolled experiments
III. Evidence from opinions of respected authorities based on clinical experience, descriptive studies, or reports of expert committees

Strength of Recommendations

A. Good evidence to support a recommendation for use
B. Moderate evidence to support a recommendation for use
C. Poor evidence to support a recommendation
D. Moderate evidence to support a recommendation against use
E. Good evidence to support a recommendation against use

CLINICAL ALGORITHM(S)

A clinical algorithm is provided in the original guideline document for "Screening for Human Immunodeficiency Virus (HIV}-related Renal Disease."

EVIDENCE SUPPORTING THE RECOMMENDATIONS

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

The type of supporting evidence is identified and graded for each recommendation (see "Major Recommendations").

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

Identification of human immunodeficiency virus (HIV)-infected patients at risk for renal disease may help clinicians implement potentially preventative and therapeutic strategies.

POTENTIAL HARMS

- Calcium channel blockers of both the dihydropyridine and nondihydropyridine classes should be used with caution because of their potential interaction with protease inhibitors, which can result in hypotension and possibly in conduction delays.
- Peritonitis has been reported in several small series of HIV-infected patients receiving peritoneal dialysis.
- Solid-organ transplantation in HIV-infected patients is complicated by drug interactions and a complex set of infectious, metabolic, and neoplastic complications related to each condition. Clinical management must be provided by a multidisciplinary team of providers who are able to communicate rapidly about evolving signs, symptoms, and laboratory abnormalities.

CONTRAINDICATIONS

CONTRAINDICATIONS

- Underlying infection would be a contraindication for immunosuppressive therapy.
- Cidofovir is contraindicated in patients with preexisting creatinine clearance of <55 mL/min or a urine protein level $\geq$2+ (100 mg/dL) on urine dipstick.

QUALIFYING STATEMENTS

QUALIFYING STATEMENTS

- Guidelines are written to improve the quality of care, to improve the appropriateness of care, to improve cost-effectiveness, and to serve as educational tools. The goal is not to create standards of care; however, other organizations may choose to adopt these guidelines or components thereof for such purposes. Practice guidelines, however, are never a substitute for clinical judgment. Clinical discretion is of the utmost importance in the application of a guideline to individual patients, because no guideline can ever be specific enough to be applied in all situations.
- Although the authors feel that these recommendations should generally apply to all human immunodeficiency virus (HIV)-infected patients, it is understood that providers need to tailor these guidelines around the needs and circumstances of the individual patient.

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

An implementation strategy was not provided.

IMPLEMENTATION TOOLS

Clinical Algorithm

For information about availability, see the "Availability of Companion Documents" and "Patient Resources" fields below.

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

Living with Illness

IOM DOMAIN

Effectiveness
Patient-centeredness

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

Gupta SK, Eustace JA, Winston JA, Boydstun II, Ahuja TS, Rodriguez RA, Tashima KT, Roland M, Franceschini N, Palella FJ, Lennox JL, Klotman PE, Nachman SA, Hall SD, Szczech LA. Guidelines for the management of chronic kidney disease in HIV-infected patients: recommendations of the HIV Medicine Association of the Infectious Diseases Society of America. Clin Infect Dis 2005 Jun 1;40(11):1559-85. [238 references] PubMed

ADAPTATION

Not applicable: The guideline was not adapted from another source.

DATE RELEASED

2005 Jun 1

GUIDELINE DEVELOPER(S)

Infectious Diseases Society of America - Medical Specialty Society

SOURCE(S) OF FUNDING

Infectious Diseases Society of America (IDSA)

GUIDELINE COMMITTEE

Infectious Diseases Society of America (IDSA) Practice Guidelines Committee

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FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

S.K.G. has received honoraria from Gilead Sciences. T.S.A. has received speaker bureau fees and funding from Genzyme. K.T.T. has received grant support and honoraria from Glaxo-SmithKline, Bristol-Myers Squibb, Gilead Sciences, and Merck. M.R. has received grant support from GlaxoSmithKline, Bristol-Myers Squibb, and Agouron Pharmaceuticals and has received honoraria from Gilead Sciences and Boehringer Ingelheim. F.J.P. has received honoraria from Bristol Myers Squibb, Roche Pharmaceuticals, Gilead Sciences, and Agouron Pharmaceuticals. J.L.L. has received grant support and honoraria from Gilead Sciences, Tibotec Pharmaceuticals, Abbott Laboratories, Merck, and Bristol- Myers Squibb. All other authors: no conflicts.

GUIDELINE STATUS

This is the current release of the guideline.

GUIDELINE AVAILABILITY

Electronic copies: Available from the Infectious Disease Society of America (IDSA) Web site:

- HTML Format
- Portable Document Format (PDF)

Print copies: Available from Infectious Diseases Society of America, 66 Canal Center Plaza, Suite 600, Alexandria, VA 22314.

AVAILABILITY OF COMPANION DOCUMENTS

The following is available:

- Kish MA. Guide to development of practice guidelines. Clin Infect Dis 2001 Mar 15;32(6):851-4.

Electronic copies: Available from the Infectious Diseases Society of America (IDSA) Web site:

- HTML Format
- Portable Document Format (PDF)

Print copies: Available from Infectious Diseases Society of America, 66 Canal Center Plaza, Suite 600, Alexandria, VA 22314.

PATIENT RESOURCES

None available

NGC STATUS

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